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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,868	06/04/2002	Hans Deckmyn	522-1778	2345

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/049,868	**Applicant(s)** DECKMYN ET AL.	
	Examiner Maher M. Haddad	**Art Unit** 1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 01 December 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *01 December 2005*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *71,75,80 and 81*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *65,66,70,72-74,82 and 83*.
   Claim(s) withdrawn from consideration: *None*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☒ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached. Term of Deposit, Dated 2/1/05

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 11. does NOT place the application in condition for allowance because: 1. Claims 70 and 83 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.
Applicant's arguments, filed 12/1/05, have been fully considered, but have not been found convincing.
The specification does not explicitly discloes that the "homolog", the "ligand" and the "CDR regions" are equivelent. The specification discloses only that homology with reference to ligands which compete with or inhibit binding of one of of the ligands. Further, the specification on page 10, lines 24-26 discloses that the homolog of antigen binding fab fragment, the CDR regions are not specifically contemplated.

2. Claims 70, 82 and 83 stand rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabled for a pharmaceutical comprosition comprising a monovalent antibody fragment which binds in vivo to human platelet glycoprotein GPIb without incurring thrombocytopenia and a pharmaceutically acceptable carrier wherein said fragment is an Fab fragment or a single variable domain or a monovalent antibody fragment which binds in vivo to human platelet glycoprotein GPIb, and prevents the binding of von Willebrand factor to human platelet glycoprotein GPIb which is an Fab fragment or a single variable domain, which inhibits platelet adhesion under high shear conditions; does not reasonably provide enablement for a pharmaceutical composition or a monovalent antibody fragment, wherein the variable region of said fragment comprises a sequence having at least 80% sequence identity with SEQ ID NO: 4 within the CDR regions as identified in Figure 13 in claims 70 and 83 , a humanized antibody fragment derivable from the monoclonal antibody . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action mailed 5/27/05.

Applicant's arguments, filed 12/1/05, have been fully considered, but have not been found convincing.

The skilled artian would not know whether the "humanized antibody fragment" refers to any antibody fragment or it is limited to fragments containing the antigen-binding domain of the antibody in claim 82.

Applicant does not dispute the teachings of Rudikoff, Panka and Amit but disagrees that those references probide basis to question the enablement of Applicant's specification as evidence of undue experimentation. however, there is tremendous variability in the importance of individual amino acids in protein sequences. Since the CDR region is a key determinants of binding specificity to human platelet glycoprotein GPIb, residue substitutions that are conservative (e.g., Glu in equilibrium Asp, Asn in equilibrium Asp, Ile in equilibrium Leu, Lys in equilibrium Arg and Ala in equilibrium Gly) can have severe phenotypic effects. There is no simple way to infer the likely effect of an amino acid substitution on the basis of sequence information alone. Therefore, one skill in the art would not be able to predicted what residue substituted/deleted/inserted in the CDR regions of the claimed antibody and still provide binding.

The claims fail to meet the enablement requirement for the "how to make and use" prongs of the U.S.C 112, 1st paragraph. The instant fact pattern fails to indicate that a representative number of structurally related antibody fragment molecule is disclosed. The artisan would not know the identity of a reasonable number of representative said fragments falling within the scope of the instant claim and consequently would not have known how to make them. Again, in order to satisfy 112, first paragraph, the specification has to teach how to make and use the antibody fragment of the invention not how to screen to identify the invention.

3. Claims 65-66, 70, 72-74 and 83 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ward et al (1995) (IDS Ref. No. C4), in view of in view of Owens et al (1994) and U.S. Pat. No. 4,731,245 for the same reasons set forth in the previous Office Action mailed 5/27/05.

Applicant's arguments, filed 12/1/05, have been fully considered, but have not been found convincing.

Applicant argues against references individually. However, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and not is it that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). See MPEP 2145. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

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